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PRE-APPEAL BRIEF REQUEST FOR REVIEW

Docket Number (Optional)
1103326-0946

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Signature /John M. Genova/

Typed or printed name John M. Genova

Application Number	Filed
10/517,869	12 October 2005
First Named Inventor	
Anders Lehmann	
Art Unit	**Examiner**
1614	Lewis, Amy A.

Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a notice of appeal.

The review is requested for the reason(s) stated on the attached sheet(s).
Note: No more than five (5) pages may be provided.

I am the

- ☐ applicant/inventor.
- ☐ assignee of record of the entire interest. See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96)
- ☑ attorney or agent of record. Registration number 32,224
- ☐ attorney or agent acting under 37 CFR 1.34. Registration number if acting under 37 CFR 1.34 _____

/John M. Genova/
Signature

John M. Genova
Typed or printed name

212-819-332
Telephone number

9 December 2008
Date

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below*.

☑ *Total of 2 forms are submitted.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants	: Anders Lehmann et al.
Serial No.	: 10/517,869
Filing or 371(c) Date	: 12 October 2005
For	: USE OF MgLUr5 ANTAGONISTS FOR THE TREATMENT OF GERD
Examiner	: Lewis, Amy A.
Group Art Unit	: 1614

CERTIFICATE OF EFS-WEB TRANSMISSION

I hereby certify that this paper is being transmitted via the Electronic Filing System to the U.S. Patent and Trademark Office on the date indicated below.

/John M. Genova/	32,224
Signature	Reg. No.
John M. Genova	9 December 2008
Signer's Name	Date

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REMARKS ACCOMPANYING
PRE-APPEAL BRIEF REQUEST FOR REVIEW

Sir:

Claims of the referenced application have been twice rejected. Pursuant to 35 U.S.C. §134(a) and 37 C.F.R. §41.31, Applicants are submitting concurrently herewith a Notice of Appeal (Form PTO/SB/31) and a Pre-Appeal Brief Request for Review (Form PTO/SB/33). Review of the rejections set forth in the *nonfinal* Office Action mailed 15 September 2008 is requested. In accordance with the relevant rules governing the Pre-Appeal Brief Conference Program, the following remarks are limited to five (5) pages.

Authorization is hereby given to charge any fee due in connection with this communication to Deposit Account No. 23-1703.

REMARKS

I. Grounds for requesting pre-appeal brief conference

In response to the *final* Office Action mailed 27 December 2007, Applicants submitted an Amendment and Request for Continued Examination under 37 C.F.R. §1.114 on 18 June 2008. The finality of that Office Action was withdrawn, and a *nonfinal* Office Action was mailed on 15 September 2008.

For the reasons set forth herein, it is respectfully submitted that the rejections of record as set forth in the *nonfinal* Office Action are without legal and/or factual basis.

II. Disposition of claims

Claims 15-28 are pending. Claims 19-23, 26 and 27 are withdrawn from consideration. Claims 15-18, 24, 25 and 28 are rejected.

III. Claim rejection – 35 U.S.C. §112: Enablement

Claims 15-18, 24, 25 and 28 are rejected under 35 U.S.C. §112, first paragraph, for lack of enablement. Each of claims 15-18 is an independent claim directed to a method for the "inhibition" or "treatment" of a specific indication. Claims 24, 25 and 28 are dependent with claims 24-25 reciting that the active ingredient of the claimed method is 2-methyl-6-(phenylethynyl)-pyridine or a hydrochloride salt thereof whereas claim 28 recites a dosage regimen for administering the claimed method.

Relying on the sentence appearing on page 2, lines 12-13 of the specification, the Examiner has construed "inhibition" and "treatment", as recited in claims 15-18, to mean "prevention". The sentence appearing on page 2, lines 12-13, provides a description of one object of the claimed invention as follows:

> The object of the present invention was to find a way for the inhibition of transient lower esophageal sphincter relaxations (TLESRs), thereby preventing reflux.

In the *final* Office Action, independent claims 17-18 reciting "prevention" were rejected for lack of enablement. The other independent claims 15-16 reciting "inhibition" or "treatment", but not "prevention", were not rejected for lack of enablement. In response to the *final* Office Action, the expression "prevention" was deleted from claims 17-18. Applicants submit that the

expansion of the lack of enablement rejection to now include claims 15-18, 24, 25 and 28 for the reasons set forth in the *nonfinal* Office Action is inconsistent with the prosecution history. Specifically, the prosecution history up to the *final* Office Action supports Applicants' position that the claimed method for the "inhibition" or "treatment" of the recited indication is enabled by the specification.

Furthermore, the outstanding lack of enablement rejection is contrary to the relevant case law. It is agreed that a claim term "must be read in view of the specification of which [it is] a part." *Phillips* v. *AWH Corp.*, 415 F.3d 1303, 1315 (Fed. Cir. 2005) (quoting *Markman* v. *Westview Instruments, Inc.*, 52 F.3d 967, 979 (Fed. Cir. 1995), aff'd 517 U.S. 370 (1996)). However, Applicants respectfully submit that the Examiner is impermissibly using the specification to read a nonexistent limitation, i.e., "prevention", into the claims. *Prima Tek II, LLC* v. *Polypap, S.A.R.L.*, 318 F.3d 1143, 1148 (Fed. Cir. 2003). None of claims 15-18, 24, 25 and 28 recites the term "prevention" and the Examiner should be prohibited from reading that term into the claims.

In conclusion, the lack of enablement rejection is not supported by the prosecution history and contravenes the relevant case law. The rejection is without factual and legal support.

IV. Claim rejection – 35 U.S.C. §112: Written Description

Claims 15-18, 24, 25 and 28 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement.

a. claim 15

Claim 15 is directed to a method for the inhibition of TLESRs by administering a therapeutically effective amount of a mGluR5 antagonist to a patient suffering from gastroesophageal reflux disease (GERD). The Examiner alleges that there is no specific connection between the preamble, i.e., a method for the inhibition of TSLERs, and administration of a mGluR5 antagonist to a patient suffering from GERD.

MPEP §2163(I) provides that a patent specification, to satisfy the written description requirement, must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. See, e.g., *Vas-Cath, Inc.* v. *Mahurkar*, 953 F.2d 1555, 1563 (Fed.Cir. 1991). The issue is, therefore,

whether the specification describes a method for inhibiting TSLERs by administering a mGluR5 antagonist to GERD patients.

- The disclosure at page 1, lines 26-28, provides that the lower esophageal sphincter ("LES") is prone to relaxing intermittently. As a result, fluid from the stomach can pass into the esophagus since the mechanical barrier is temporarily lacking or deficient. Such events are understood throughout the specification as "reflux".
- The publication Holloway & Dent, Gastroenterol. Clin. N. Amer. 19, pp 517-535 (1990) (hereinafter "Holloway & Dent") is cited on page 2, lines 1-3 of the specification, in support of the knowledge at the time the claimed invention was made that "most reflux episodes occur during...TSLERs..." Similarly, on page 4 of the *final* Office Action, the Examiner acknowledges that it is well established that TSLERs is a dominant characteristic of GERD.
- On page 5 of the *final* Office Action, the Examiner acknowledges that the Examples, in particular the Tables on page 11 of the specification, demonstrate a percent inhibition of TSLERs in an animal model following the administration of a mGluR5 antagonist.
- A regimen for administering a therapeutically effective amount of mGluR5 antagonist is disclosed on page 8, lines 17-24 of the specification.
- The following statement appearing at page 2, lines 21-23 of the specification, describes a causal relation between the preamble, i.e., a method for the inhibition of TSLERs, and administration of a mGluR5 antagonist to a patient suffering from GERD:

  > It has now surprisingly been found that ... mGluR5 antagonists are useful for the inhibition of ...TSLERs, ***and thus for the treatment of...GERD***.

In view of the foregoing, Applicants submit that each and every feature of independent claim 15 and dependent claims 24, 25 and 28 is adequately described in the specification. The inhibition of TSLERs by the administration of a mGluR5 antagonist is useful in the treatment of GERD patients. Withdrawal of the §112 rejection is requested.

b. claims 16-18

Claim 16 is directed to a method for the treatment of GERD by administering a

therapeutically effective amount of a mGluR5 antagonist to a patient suffering from GERD. Reflux (claim 17) and regurgitation (claim 18) are symptoms of GERD.

The specification defines reflux to mean an episode when the LES is relaxing intermittently (See p. 1, lines 26-28). The publication Holloway & Dent cited on page 2, lines 1-3 of the specification indicates that "most reflux episodes occur during...TSLERs..." Similarly, on page 4 of the *final* Office Action, the Examiner acknowledges that it is well established that TSLERs is a dominant characteristic of GERD. It is undisputed that the specification supports the efficacy of mGluR5 antagonists in inhibiting TSLERs. At page 2, lines 21-23 of the specification, the written description provides a statement of Applicants' discovery of the connection between the inhibition of TSLERs – and thus treatment of GERD - by administering a mGluR5 antagonist.

In view of the foregoing, Applicants submit that each and every feature of independent claims 16-18 and dependent claims 24, 25 and 28 is adequately described in the specification. Withdrawal of the §112 rejection is requested.

V. Claim rejection – 35 U.S.C. §112: Indefiniteness

Claims 15-18, 24, 25 and 28 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Again, on page 4 of the *nonfinal* Office Action, the Examiner alleges that there is no specific connection with the preamble, i.e., a method for the inhibition of TSLERs, with the administration of a mGluR5 antagonist to a patient suffering from GERD. According to the Examiner, it is unclear if the patients being treated have TSLERs with or without GERD.

The indefiniteness rejection and the Examiner's rationale are untenable in view of the comments in the preceding Section IV. Briefly, the LES is prone to relaxing intermittently, thus giving rise to the reflux or regurgitation of gastric juice into the esophagus. At the time the claimed invention was made, it was known that most reflux episodes occur during TSLERs. The specification discloses that the administration of a mGluR5 antagonist inhibits TSLERs and is thus useful for the treatment of GERD.

Applicants submit that there is no ambiguity. In accordance with the claimed invention, the administration of a mGluR5 antagonist is useful in the inhibition of TSLERs and thus for the treatment of GERD and its symptoms, e.g., reflux and regurgitation.

VI. Request for withdrawal of the election of species requirement

Applicants were required to elect a single mGluR5 antagonist species. With traverse, Applicants elected 2-methyl-6-(phenylethynyl)-pyridine ("MPEP") for the purpose of initiating substantive examination. The election of species requirement was made final. The Examiner maintains that an examination of more than just the elected species MPEP would present an undue burden on the Examiner.

Basic fairness requires that the alleged burden on the Examiner be compared to Applicants' contribution to the pharmaceutical sciences. The claimed invention represents an important contribution to the medical and pharmaceutical sciences in providing a new and advantageous method of treating and providing relief to GERD patients. Applicants are the first to discover that mGluR5 antagonists are useful for the inhibition of TSLERs and thus for the treatment of GERD. The therapeutic benefit of Applicants' invention is more than the administration of a single elected species. As such, it is respectfully submitted that the election of species requirement undermines the patent system which is constitutionally mandated to promote the useful arts and sciences.

A prior art search has not yet been performed. The specification at page 1, lines 15-17 clearly indicates that this subtype of mGluR5 antagonists is characterized by their function, i.e., their interaction with the metabotropic glutamate receptor 5. In view of this commonality, it is respectfully submitted that any burden on the Examiner to perform a prior art search of the genus of mGluR5 antagonists is outweighed by Applicants' expense and the public's detriment stemming from a protracted examination based on an arbitrary sorting of species. Withdrawal of the election of species requirement is requested. Basic fairness to Applicants and the public favor an examination of the genus of mGluR5 antagonists in the present application.

Dated: 9 December 2008

Respectfully submitted,

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